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L1          63151 S 901219-910731/PD
                SET HIG ON
L2           2415 S HYBRIDI?
L3            310 S L1 AND L2
                SET PAG 24
                SET PAG SCR

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1. 5,023,243, Jun. 11, 1991, Oligonucleotide therapeutic agent and method of making same; Richard H. Tullis, 514/44; 435/91; 536/27; 935/34

US PAT NO: 5,023,243 L1: 1 of 1

CLAIMS:

CLMS(1)

I claim:

1. A method of selectively inhibiting in vivo synthesis of one or more specific targeted proteins without substantially inhibiting the synthesis of non-targeted proteins, comprising the steps of:
synthesizing an aligodeoxyribonucleotide having a nucleotide sequence substantially complementary to at least a portion of the base sequence of messenger ribonucleic acid coding for said targeted protein,
at least a portion of said oligodeoxyribonucleotide being in the form of a phosphotriester to limit degradation in vivo;
introducing said stable oligodeoxyribonucleotide into a cell; and
hybridizing said stable oligodeoxyribonucleotide with said base sequence of said messenger ribonnucleic acid coding for said targeted protein, whereby translation of said base sequence is substantially blocked and synthesis of said targeted protein is inhibited.

CLMS(2)

2. The method of claim 1, wherein said oligodeoxyribonucleotide comprises at least 14 nucleotides.

CLMS(3)

3. The method of claim 1, wherein said oligodeoxyribonucleotide comprises about 23 nucleotides.

CLMS(4)

4. The method of claim 1, wherein said targeted protein is follicle stimulating hormone, which has an alpha chain and a beta chain.

CLMS(5)

5. The method of claim 4, wherein the oligodeoxyribonucleotide comprises the nucleotide sequence from 5' to 3' of GTGTAGCAGTAR.sub.1 CCR.sub.2 GCGCACCA, and wherein R.sub.1 is G or T and R.sub.2 is G or T.

CLMS(6)

6. The method of claim 1, wherein said hybridization occurs at about 37.degree. C.

CLMS(7)

7. The method of claim 1, wherein said oligodeoxyribonucleotide is formed through diester bonding.

CLMS(8)

8. A method of controlling the infection of a host organism by a foreign

vital to the foreign organism's viability, comprising the steps of:
determining the base sequence of the foreign organism's nucleic acid, said base sequence coding for at least a portion of said protein vital to the foreign organism's viability;
synthesizing an oligodeoxyribonucleotide the order of nucleotides being substantially complementary to a portion of the foreign organism's messenger ribonucleic acid coding for said protein vital to said foreign organism's viability,
at least a portion of said oligodeoxyribonucleotide being in the form of a phosphotriester to inhibit degradation in vivo;
introducing said oligodeoxyribonucleotide into the cells of said host organism; and
hybridizing said oligodeoxyribonucleotide with said portion of the foreign organism's messenger ribonucleic acid so as to substantially block translation of said foreign organism's messenger ribonucleic acid coding for said protein, thereby inhibiting synthesis of said protein vital to the viability of the foreign organism.

CLMS(9)

9. The method of claim 8 further comprising the step of:
determining the order of the base sequence of said organism's nucleic acid prior to synthesizing the oligodeoxyribonucleotide.

CLMS(10)

10. The method of claim 8 further comprising the step of:
cross-hybridizing the oligodeoxyribonucleotide against messenger ribonucleic acid from at least one species different from said foreign organism and selecting that fraction of the oligodeoxyribonucleotide which does not so hybridize so as to increase the specificity of the selected oligodeoxyribonucleotide against said foreign organism.

CLMS(11)

11. The method of claim 10, wherein said cross-hybridization is performed against messenger ribonucleic acid from said host organism.

CLMS(12)

12. The method of claim 10, wherein the selected oligodeoxyribonucleotide substantially hybridizes only with a messenger ribonucleic acid unique to said foreign organism.

CLMS(13)

13. A genetically engineered therapeutic process which inhibits synthesis of one or more targeted proteins within the cells of an organism without substantially inhibiting synthesis of non-targeted proteins, comprising the steps of:
determining the base sequence of the messenger ribonucleic acid coding for the targeted protein;
synthesizing an oligodeoxyribonucleotide having a nucleotide sequence substantially complementary to the region of the messenger ribonucleic acid coding for said targeted protein,
at least a portion of said oligodeoxyribonucleotide being in the form of a phosphotriester to inhibit degradation in vivo;
introducing said oligodeoxyribonucleotide into the cells of said organism; and
hybridizing said oligodeoxyribonucleotide with said base sequence of said messenger ribonucleic acid coding for said targeted protein, whereby translation of said base sequence is substantially blocked and synthesis of said targeted protein is inhibited.

CLMS(14)

14. A method of developing oligodeoxyribonucleotide therapeutic agents for use in vivo inhibition of the synthesis of one or more targeted proteins in a cell without substantially inhibiting the synthesis of non-targeted proteins, comprising the steps of:

determining the base sequence of an organism's messenger ribonucleic acid, said base sequence coding for at least a portion of said protein targeted for inhibition;

synthesizing an oligodeoxyribonucleotide, the nucleotide sequence of which is substantially complementary to at least a portion of said base sequence,

at least a portion of said oligodeoxyribonucleotide being in the form of a phosphotriester in order to limit degradation in vivo, whereby said oligodeoxyribonucleotide may be introduced into the cells of said organism for hybridization with said messenger ribonucleic acid base sequence coding for at least a portion of said protein targeted for inhibition so as to substantially block translation of said base sequence and inhibit synthesis of said targeted protein;

cross hybridizing said oligodeoxyribonucleotide against messenger ribonucleic acid from at least one species different from said organism; and

selecting that fraction of the oligoribonucleotide which does not so hybridize so as to increase the specificity of the selected oligodeoxyribonucleotide to messenger ribonucleic acid unique to said organism.

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